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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/618,088

07/14/2003

Elizabeth Jaffee

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BANNER & WITCOFF, LTD.

1100 13th STREET, N.W.

SUITE 1200

WASHINGTON, DC 20005-4051

EXAMINER

GUSSOW, ANNE

ART UNIT

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1643

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/618,088	<b>Applicant(s)</b> JAFEE ET AL.	
	<b>Examiner</b> ANNE M. GUSSOW	<b>Art Unit</b> 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 August 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 22-34,37,38,111 and 114-121 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 22-25,27-34,37,111,114 and 116-121 is/are rejected.
- 7) ☒ Claim(s) 26 38 115 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Claims 22, 29, 38, 114, and 121 have been amended.  
Claims 35, 36, 112, and 113 have been canceled.
2. In searching for the species of pancreatic cancer the examiner found art which reads upon the other species of squamous cell carcinoma, ovarian cancer and mesothelioma. Thus, the species election is WITHDRAWN.
3. Claims 22-34, 37, 38, 111, and 114-121 are under examination.
4. The following Office Action contains NEW GROUNDS of Rejection.

### ***Rejections Withdrawn***

5. The rejection of claims 22-24, 26-38, 111, 113-115, 117-119, and 121 under 35 U.S.C. 112, first paragraph as lacking enablement is withdrawn in view of applicant's amendment to the claims.

### ***NEW GROUNDS of Rejection***

#### ***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 38 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

The response filed August 14, 2008 has introduced NEW MATTER into the claims. Newly amended claim 38 recites that the composition is administered in an amount sufficient to keep the patient tumor-free greater than 60 months. The response pointed to Table 2 to provide support for amended claim 38 in the originally filed disclosure. Table 2 discloses mesothelin for the treatment of pancreatic cancer, which doesn't support the broader scope of the instant claim. Further, only three of the 14 patients shown in Table 2 support the patient being tumor free greater than 60 months. Instant claim 38 now recites limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in claim 38, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in present claim 38 in the specification or claims, as-filed, or remove these limitations from the claims in response to this Office Action.

***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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11. Claims 22-25, 27-31, 34, 37, 111, 114, 116-121 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weiskirch and Paterson (Immunological Reviews, 1997. Vol. 158, pages 159-169) in view of Argani, et al. (Clinical Cancer Research, 2001. Vol. 7, pages 3862-3868, as cited on the IDS filed September 11, 2003).

The claims recite a method of inducing a T-cell response to a tumor which overexpresses mesothelin relative to normal tissue from which it is derived, said method comprising: administering to a patient who has said tumor or who has had said tumor removed, a composition comprising a *Listeria monocytogenes* bacterium which expresses a polypeptide comprising an MHC Class I-binding epitope of mesothelin, wherein the epitope binds to an allelic form of MHC class I which is expressed by the patient, whereby a T-cell response to mesothelin is induced, wherein the tumor is selected from the group consisting of ovarian cancer, pancreatic cancer, mesothelioma, and squamous cell carcinoma.

Weiskirch and Paterson teach generation of a T-cell immune response to the nucleoprotein gene of influenza by administering a *Listeria monocytogenes* construct that expressed either the full length protein or a truncated form of the protein. Weiskirch and Paterson teach mice generated a MHC class I restricted immune response to the nucleoprotein. Weiskirch and Paterson teach the induction of an immune response to be useful for treating cancer or viral infection (see entire document, particularly page 163 and figure 2). Weiskirch and Paterson teach administration of an attenuated strain was as effective as administration of a live *Listeria monocytogenes* strain (see figure 4

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and page 162 2<sup>nd</sup> column). Weiskirch and Paterson do not teach mesothelin protein.

This deficiency is made up for in the teachings of Argani, et al.

Argani, et al. teach mesothelin is a membrane-bound protein and is expressed in a variety of cancers including squamous carcinomas of the esophagus, lung, cervix, malignant mesothelioma, ovarian and pancreatic carcinoma (see Introduction) and cell-mediated immunotherapy can be safe and effective in patients with pancreatic cancer (page 3867, 2nd column).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have induced a T-cell immune response for cancer treatment by administering the *Listeria monocytogenes* construct of Weiskirch and Paterson which expressed the mesothelin protein as taught by Argani, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have induced a T-cell immune response for cancer treatment by administering the *Listeria monocytogenes* construct of Weiskirch and Paterson which expressed the mesothelin protein as taught by Argani, et al. because Argani, et al. teach that mesothelin is a membrane bound protein that is expressed on a number of cancer types including squamous carcinomas of the esophagus, lung, cervix, malignant mesothelioma, ovarian and pancreatic carcinoma and cell-mediated immunotherapy can be safe and effective in patients with pancreatic cancer. Additionally, regarding treatment after surgery, one of ordinary skill in the art would know to use the construct of Weiskirch and Paterson after surgically removing the tumor to remove any remaining cancerous cells in the patient. Thus, it would have been

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obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the *Listeria monocytogenes* construct of Weiskirch and Paterson and express the mesothelin protein for T cell-mediated immunotherapy and therapeutic benefit in patients suffering from cancers of the esophagus, lung, cervix, ovarian, pancreatic, mesothelioma, and squamous cell carcinoma in view of Argani, et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

12. Claims 22-25, 27-34, 37, 111, 114, and 116-121 rejected under 35 U.S.C. 103(a) as being unpatentable over Weiskirch and Paterson (Immunological Reviews, 1997. Vol. 158, pages 159-169) in view of Argani, et al. (Clinical Cancer Research, 2001. Vol. 7, pages 3862-3868, as cited on the IDS filed September 11, 2003) and in view of Schirle, et al. (Journal of Immunological Methods, 2001. Vol. 257, pages 1-16).

Claims 22-25, 27-31, 34, 37, 111, 114, and 116-121 have been described supra. Claims 32-33 recite wherein the polypeptide is selected as being an MHC class-I binding epitope using an algorithm.

Weiskirch and Paterson has been described supra. Weiskirch and Paterson do not teach mesothelin protein or an algorithm. These deficiencies are made up for in the teachings of Argani, et al. and Schirle, et al.

Argani, et al. has been described supra.

Schirle, et al. teach the use of computer algorithms to predict epitopes for MHC class I and class II molecules (see entire document).



It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have induced a T-cell immune response for cancer treatment by administering the *Listeria monocytogenes* construct of Weiskirch and Paterson which expressed the mesothelin protein as taught by Argani, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have induced a T-cell immune response for cancer treatment by administering the *Listeria monocytogenes* construct of Weiskirch and Paterson which expressed the mesothelin protein as taught by Argani, et al. because Argani, et al. teach that mesothelin is a membrane bound protein that is expressed on a number of cancer types including squamous carcinomas of the esophagus, lung, cervix, malignant mesothelioma, ovarian and pancreatic carcinoma and cell-mediated immunotherapy can be safe and effective in patients with pancreatic cancer. Additionally, Schirle, et al. teach multiple algorithms available for determining MHC class I peptides (see page 4 and table 1). Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the *Listeria monocytogenes* construct of Weiskirch and Paterson and express the mesothelin protein for T cell-mediated immunotherapy and therapeutic benefit in patients suffering from cancers of the esophagus, lung, cervix, ovarian, pancreatic, mesothelioma, and squamous cell carcinoma in view of Argani, et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

***Conclusions***

13. Claims 26, 38, and 115 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

14. Claims 22-25, 27-34, 37, 111, 114, and 116-121 are rejected.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

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USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow

November 20, 2008

/David J Blanchard/  
Primary Examiner, Art Unit 1643